

GEORGIA INSTITUTE OF TECHNOLOGY  
OFFICE OF CONTRACT ADMINISTRATION  
SPONSORED PROJECT INITIATION

Date: February 29, 1980

Project Title: The Chemistry of New Functional Groups In Enzymes

Project No: G-33-N02

Project Director: Dr. Edward M. Burgess

Sponsor: DHEW/PHS/NIH - National Institute of General Medical Sciences;  
Bethesda, Maryland 20014

Agreement Period: From March 1, 1980 Until February 28, 1981 (10 year)

Type Agreement: Grant No. 5-R01-GM12672-10

Amount: \$87,722 New PHS Funds (G-33-N02)  
8,731 GIT Contribution (G-33-355)  
\$96,453 Total

Reports Required: Annual Progress Reports with Continuation Applications; Terminal  
Progress Report upon Grant Expiration

Sponsor Contact Person (s):

Technical Matters

Dr. Carl A. Keuther  
Program Administrator  
National Institute of General Medical  
Sciences  
Bethesda, Maryland 20014  
  
(301) 496-7181

Contractual Matters

(thru OCA)

K. McKnight  
Grants Management Specialist  
Office of Associate Director for  
Program Activities  
National Institute of General Medical  
Sciences  
Bethesda, Maryland 20014

(301) 496-7166

NOTE: Continuation of G-33-678 (07 & 08 Budget Periods) & G-33-N01 (09 Budget Period)

Defense Priority Rating: None

Assigned to: Chemistry (School/Laboratory)

COPIES TO:

Project Director  
Division Chief (EES)  
School/Laboratory Director  
Dean/Director-EES  
Accounting Office  
Procurement Office  
Security Coordinator (OCA)  
Reports Coordinator (OCA)

Library, Technical Reports Section  
EES Information Office  
EES Reports & Procedures  
Project File (OCA)  
Project Code (GTRI)  
Other \_\_\_\_\_

21  
58-227

GEORGIA INSTITUTE OF TECHNOLOGY  
OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION

Date: 2/24/81

Project Title: The Chemistry of New Functional Groups in Enzymes

Project No: G-33-N02

Project Director: Dr. Edward M. Burgess

Grant # 5-R01-GM12672-10

Sponsor: DHEW/PHS/NIH - National Institute of General Medical Sciences;  
Bethesda, Maryland 20014

Effective Termination Date: 2/28/81 (year 10)

Clearance of Accounting Charges: \_\_\_\_\_

Grant/Contract Closeout Actions Remaining:

- ☐ Final Invoice and Closing Documents
- ☐ Final Fiscal Report
- ☒ Final Report of Inventions
- ☐ Govt. Property Inventory & Related Certificate
- ☐ Classified Material Certificate
- ☒ Other Annual Report of Expenditures due by 5/31/81

NOTE: Follow-On Project (11 year) is G-33-N03

Assigned to: Chemistry (School/~~Laboratory~~)

COPIES TO:

Project Director  
Division Chief (EES)  
School/Laboratory Director  
Dean/Director-EES  
Accounting Office  
Procurement Office  
Security Coordinator (OCA)  
~~Reports Coordinator (OCA)~~

Library, Technical Reports Section  
EES Information Office  
Project File (OCA)  
Project Code (GTRI)  
Other OCA Research Project Coordinator

APPLICANT: REPEAT GRANT NUMBER SHOWN ON PAGE 1 →		GRANT NUMBER	
<b>SECTION IV—SUMMARY PROGRESS REPORT</b>		GM 12672-11	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial)		PERIOD COVERED BY THIS REPORT	
Burgess, Edward M.		FROM	THROUGH
NAME OF ORGANIZATION		3/1/80	2/28/81
Georgia Institute of Technology			
TITLE (Repeat title shown in Item 1 on first page)			
The Chemistry of New Functional Groups in Enzymes			

1. List publications: (a) published and not previously reported; (b) in press. Provide five reprints if not previously submitted.
2. List all additions and deletions in professional personnel and any changes in effort.
3. Progress Report. (See Instructions)

1. None

2. Professional Personnel

Deletions:

Van Derveer, Donald  
Campbell, D. C.

Postdoctoral Assoc.  
Research Assistant

terminated 2-29-80  
terminated 6-1-80

Additions:

Zoller, Uri

Postdoctoral Assoc.

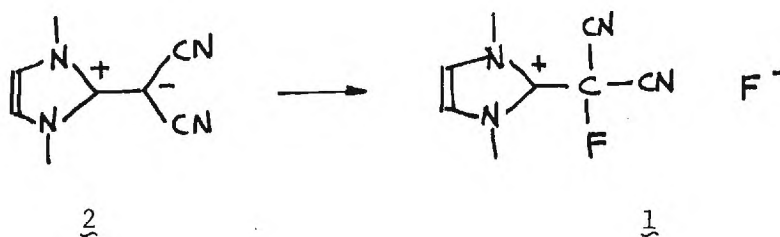
8-1-80

3. Progress Report:

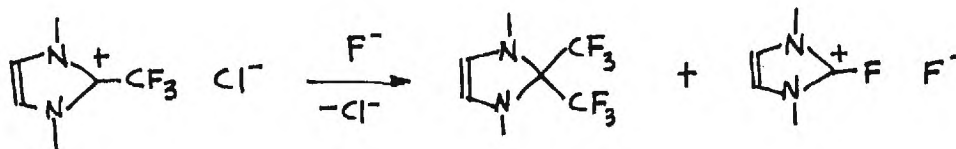
The numbering of topics in this report follows from our proposal.

1. Hypervalent First and Second Row Molecules.

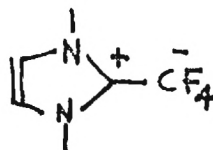
The structure of the product, 1, resulting from the reaction of the 1,2-dipole, 2, with  $\text{CF}_3\text{OF}$  has been determined by NMR  $\text{F}^{19}$  spectroscopy to have non-equivalent fluorines. This would seem to end our search



for hypervalent carbon. In one last attempt, we carried out the following reaction and obtained the result indicated.



No evidence for the hypervalent species, 3, was forthcoming.

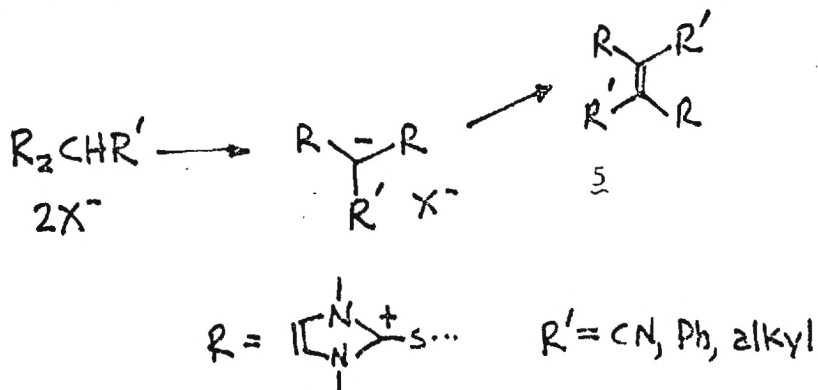


3

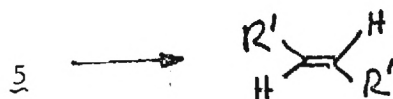
## 2. Thione Ylides

### (a.) Ylides from Bis-thioimidazolium salts.

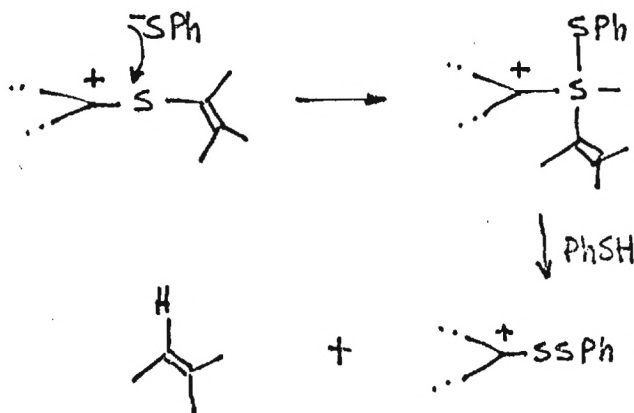
The reaction of gem-dihalides with dimethylimidazolethione give the corresponding bis-salts, 4, whose base catalyzed decomposition give the substituted ethylene derivatives, 5, at temperatures of 30-80°.



This coupling reaction would have some synthetic utility if the following transformation of the produce 5 could be developed.



and we are currently studying the reaction of 5 with "soft" nucleophiles such as PhSH, PhS<sup>-</sup> or PhSeH, PhSe<sup>-</sup> with the hope of finding a reaction:

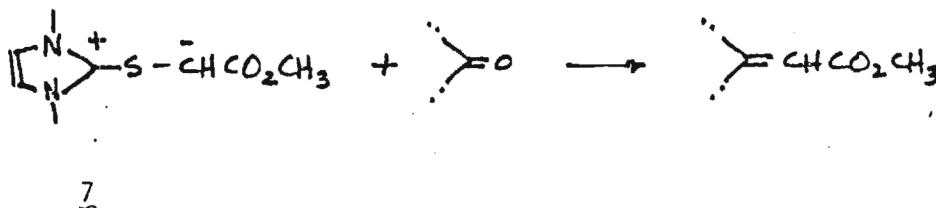




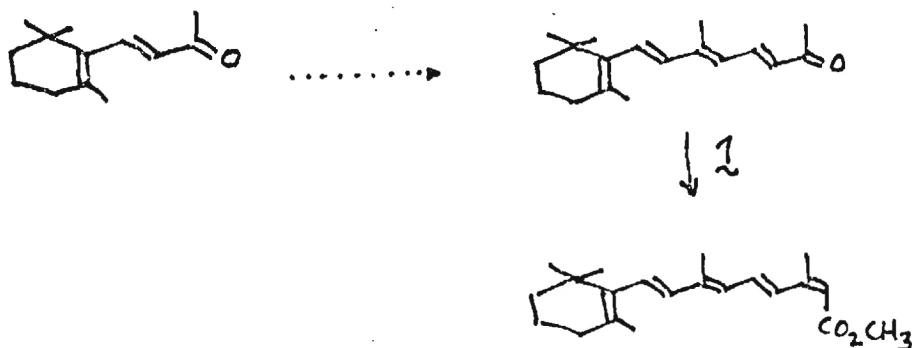
3. Synthetic Application of Hypervalent Intermeidates

## (a.) Thione Methylides

We have discovered the reaction conditions (time, temperature) which effect the "pseduo" wittig reaction of 1 with ketones (formerly only a reagent for aldehydes).

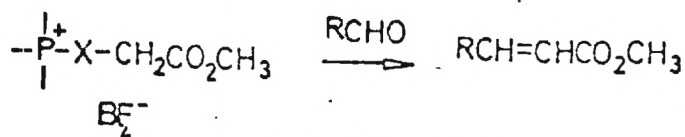
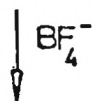
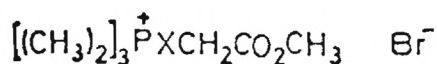
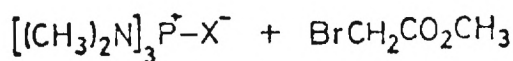


This will allow us to proceed toward the synthesis of the important agent (for severe acne and possibly useful as an antineoplastic agent) 13-cis-retenoic acid. We have begun, as follows:



## (b.) Phosphile Sulfide and Selenide Methylides

We have extended out studies on the reaction of the title ylides with aldehydes and found the stereochemistry of the acrylate ester product to be a function of the method of generating the ylide (below).



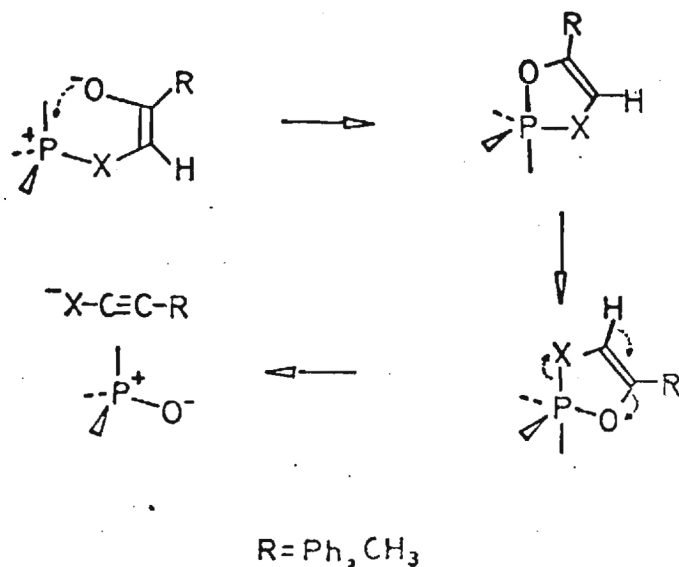
- A. DBU,  $CH_3CN$   
 B. DBU,  $CH_3CN$ , LiI  
 C. NaOH,  $H_2O$ ,  $CH_2Cl_2$ ,  $Et_3BuN^+Cl^-$   
 D. NaOEt, EtOH

R=Ph

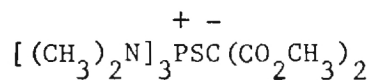
	X = S		X = Se	
	Z	E	Z	E
A	60	40	60	40
B	75	25	98	2
C	70	30	50	50
D	0	100	50	50

Thus, a stereospecific formation of either isomer may be selected using as variables the central atom of the ylides or its method of preparation. Interestingly, ylides generated with ketone stabilizing substituents (rather than ester) undergo the following internal rearrangement and fragmentation faster than reaction with

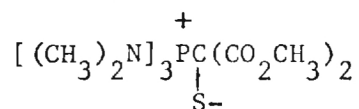
an external aldehyde. We can offer no explanation for this.



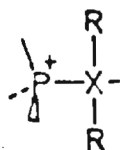
In another study, we attempted the isolation of a phosphine sulfide methylyde,



however, after a few hours in solution this ylide underwent rearrangement to

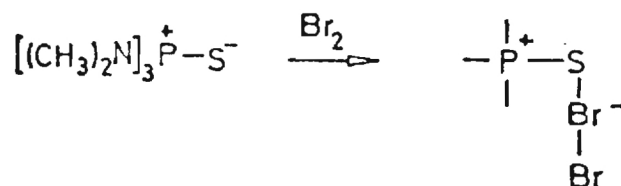


Finally, in an attempt to generate an isolable hypervalent species:





we subjected tri-dimethylaminophosphine sulfide to bromination. The product isolated and characterized by x-ray crystallography is shown below.



The undersigned agrees to accept responsibility for the scientific and technical conduct of the project and for provision of required progress reports if a grant is awarded as the result of this application.

12-16-80

Date

Edward H. Bengers  
Principal Investigator